

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims:

1 - 25 (canceled).

26 (previously presented). The method of claim 161, wherein said sequence alteration is a substitution of at least one base.

27 (previously presented). The method of claim 161, wherein said sequence alteration is a deletion of at least one base.

28 (previously presented). The method of claim 161, wherein said alteration is an insertion of at least one base.

29 - 32 (canceled).

33 (previously presented). The method of claim 161, wherein said chromosome is an artificial chromosome.

34 (canceled).

35 (previously presented). The method of claim 161, wherein said cellular repair proteins are purified.

36 (previously presented). The method of claim 161, wherein said cellular repair proteins are present in a cell-free protein extract.

37 (previously presented). The method of claim 161, wherein said cellular repair proteins are present within an intact cell.

38 (previously presented). The method of claim 37, wherein said cell is cultured *ex vivo*.

39 (canceled).

40 (previously presented). The method of claim 161, wherein said cellular repair proteins are of a cell selected from the group consisting of: prokaryotic cells and eukaryotic cells.

41 (previously presented). The method of claim 40, wherein said cell is a prokaryotic cell.

42 (previously presented). The method of claim 41, wherein said prokaryotic cell is a bacterial cell.

43 (previously presented). The method of claim 42, wherein said bacterial cell is an *E. coli* cell.

44 (previously presented). The method of claim 40, wherein said cell is a eukaryotic cell.

45 (previously presented). The method of claim 44, wherein said eukaryotic cell is a yeast cell, plant cell, human cell, or a mammalian cell.

46 (previously presented). The method of claim 45, wherein said eukaryotic cell is a yeast cell.

47 (previously presented). The method of claim 46, wherein said yeast cell is a *Saccharomyces cerevisiae*, *Ustilago maydis*, or *Candida albicans* cell.

48 (previously presented). The method of claim 45, wherein said eukaryotic cell is a plant cell.

49 (previously presented). The method of claim 45, wherein said eukaryotic cell is a human cell.

50 (previously presented). The method of claim 49, wherein said human cell is selected from the group consisting of liver cell, lung cell, colon cell, cervical cell, kidney cell, epithelial cell, cancer cell, and stem cell.

51 (previously presented). The method of claim 45, wherein said eukaryotic cell is from a mammal.

52 (previously presented). The method of claim 51, wherein said mammal is selected from the group consisting of: rodent, mouse, hamster, rat, and monkey.

53 (previously presented). The method of claim 161, wherein said oligonucleotide is at least 25 nucleotides in length.

54 (previously presented). The method of claim 161, wherein said oligonucleotide is no more than 74 nucleotides in length.

55 (canceled).

56 (previously presented). The method of claim 161, wherein said first strand is the nontranscribed strand of the target nucleic acid.

57 (currently amended). The method of claim 161, wherein the sequences of said ~~deoxyribonucleotide~~ unmodified DNA domain and of the target nucleic acid first strand are mismatched at a single nucleotide.

58 (currently amended). The method of claim 161, wherein the sequences of said ~~deoxyribonucleotide~~ unmodified DNA domain and of its complement on the target nucleic acid first strand are mismatched at two or more nucleotides.

59 (previously presented). The method of claim 161, wherein said at least one terminal modification is at least one 3' terminal LNA analogue.

60 (previously presented). The method of claim 59, wherein said oligonucleotide has no more than 3 LNA analogues at its 3' terminus.

61 (previously presented). The method of claim 59, wherein said oligonucleotide has at least one LNA at its 3' terminus and at least one LNA at its 5' terminus.

62 (previously presented). The method of claim 61, wherein said oligonucleotide has no more than 3 contiguous LNA at each of its 3' or 5' termini.

63 (previously presented). The method of claim 161, wherein said at least one terminal modification is at least one 2'-O-methyl ribonucleotide analog at its 3' terminus.

64 (previously presented). The method of claim 63, wherein said oligonucleotide has no more than 4 contiguous 2'-O-methyl ribonucleotide analogs.

65 (previously presented). The method of claim 63, wherein said oligonucleotide has at least one 2'-O-methyl ribonucleotide analog at its 3' terminus and at least one 2'-O-methyl ribonucleotide analog at its 5' terminus.

66 (previously presented). The method of claim 65, wherein said oligonucleotide has no more than 4 contiguous 2'-O-methyl ribonucleotide analogs.

67 (previously presented). The method of claim 161, wherein said at least one terminal modification comprises at least three terminal phosphorothioate linkages.

68 (previously presented). The method of claim 67, wherein said phosphorothioate linkages at said oligonucleotide's 3' terminus.

69 (previously presented). The method of claim 67, wherein said oligonucleotide comprises no more than 6 contiguous phosphorothioate linkages.

70 (currently amended). A method of targeted sequence alteration of a nucleic acid present within selectively enriched cells *in vitro*, cells in culture, or cell-free extracts, comprising:

~~combining~~ contacting the targeted nucleic acid in the presence of cellular repair proteins with a single-stranded nonhairpin oligonucleotide 17 - 121 nucleotides in length, said oligonucleotide having a domain of at least 8 contiguous deoxyribonucleotides,

wherein said oligonucleotide is fully complementary in sequence to the sequence of a first strand of the targeted nucleic acid ~~target~~, but for one or more mismatches as between the sequences of said deoxyribonucleotide domain and its complement on the target nucleic acid first strand, each of said mismatches positioned at least 8 nucleotides from said oligonucleotide's 5' and 3' termini;

wherein said oligonucleotide has at least one terminal modification selected from the group consisting of: at least one terminal locked nucleic acid (LNA), at least one terminal 2'-O-Me base analog, and at least three terminal phosphorothioate linkages;

wherein said cultured or selectively enriched cells are not human embryonic stem cells, and

wherein said targeted nucleic acid is selected from the group of human genes consisting of: ADA, p53, beta-globin, RB, BRCA1, BRCA2, CFTR, CDKN2A, APC, Factor V, Factor VIII, Factor IX, hemoglobin alpha 1, hemoglobin alpha 2, MLH1, MSH2, MSH6, ApoE, LDL receptor, UGT1, APP, PSEN1, and PSEN2.

71 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human beta-globin gene.

72 (previously presented). The method of claim 71, wherein said human beta-globin gene is targeted in a human hematopoietic stem cell.

73 (currently amended). A method of targeted sequence alteration of a nucleic acid present within selectively enriched cells in vitro, cells in culture, or cell-free extracts, comprising:

~~combining~~ contacting the targeted nucleic acid in the presence of cellular repair proteins with a single-stranded nonhairpin oligonucleotide 17 - 121 nucleotides in length, said oligonucleotide having a domain of at least 8 contiguous deoxyribonucleotides,

wherein said oligonucleotide is fully complementary in sequence to the sequence of a first strand of the targeted nucleic acid-~~target~~, but for one or more mismatches as between the sequences of said deoxyribonucleotide domain and its complement on the target nucleic acid first strand, each of said mismatches positioned at least 8 nucleotides from said oligonucleotide's 5' and 3' termini;

wherein said oligonucleotide has at least one terminal modification selected from the group consisting of: at least one terminal locked nucleic acid (LNA), at least one terminal 2'-O-Me base analog, and at least three terminal phosphorothioate linkages;

wherein said cultured or selectively enriched cells are not human embryonic stem cells, and

wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 1 - 4340.

74 (previously presented). The method of claim 73, wherein said oligonucleotide has sequence identical to any one of SEQ ID NOS: 1 - 4340.

75 (currently amended). A method of targeted sequence alteration of a nucleic acid present within selectively enriched cells in vitro, cells in culture, or cell-free extracts, comprising:

~~combining~~ contacting the targeted nucleic acid in the presence of cellular repair proteins with a single-stranded nonhairpin oligonucleotide 17 - 121 nucleotides in length, said oligonucleotide having a domain of at least 8 contiguous deoxyribonucleotides,

wherein said oligonucleotide is fully complementary in sequence to the sequence of a first strand of the targeted nucleic acid ~~target~~, but for one or more mismatches as between the sequences of said deoxyribonucleotide domain and its complement on the target nucleic acid first strand, each of said mismatches positioned at least 8 nucleotides from said oligonucleotide's 5' and 3' termini;

wherein said oligonucleotide has at least one terminal modification, said oligonucleotide includes the sequence of any one of SEQ ID NOs: 1 - 4340, and said cultured or selectively enriched cells are not human embryonic stem cells.

76 (previously presented). The method of claim 75, wherein said at least one terminal modification is selected from the group consisting of: at least one terminal locked nucleic acid (LNA), at least one terminal 2'-O-Me base analog, and at least three terminal phosphorothioate linkages.

77 (previously presented). The method of claim 75, wherein said target is chromosomal genomic DNA.

78 (currently amended). A method of targeted sequence alteration of a nucleic acid present within selectively enriched hematopoietic stem cells in vitro or hematopoietic stem cells in culture, comprising:

~~combining~~ contacting the targeted nucleic acid in the presence of cellular repair proteins with a single-stranded nonhairpin oligonucleotide 17 - 121 nucleotides in length, said oligonucleotide having a domain of at least 8 contiguous deoxyribonucleotides,

wherein said oligonucleotide is fully complementary in sequence to the sequence of a first strand of the targeted nucleic acid ~~target~~, but for one or more mismatches as between the sequences of said deoxyribonucleotide domain and its complement on the target nucleic acid first strand, each of said mismatches positioned at least 8 nucleotides from said oligonucleotide's 5' and 3' termini; and

wherein said oligonucleotide has at least one terminal modification selected from the group consisting of: at least one terminal locked nucleic acid (LNA), at least one terminal 2'-O-Me base analog, and at least three terminal phosphorothioate linkages.

79 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human ADA gene.

80 (previously presented). The method of claim 79, wherein said ADA gene is targeted in a human hematopoietic stem cell.

81 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human p53 gene.

82 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human RB gene.

83 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human BRCA1 gene.

84 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human BRCA2 gene.

85 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human CFTR gene.

86 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human CDKN2A gene.

87 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human APC gene.

88 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human Factor V gene.

89 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human Factor VIII gene.

90 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human Factor IX gene.

91 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human hemoglobin alpha 1 gene.

92 (previously presented). The method of claim 91, wherein said hemoglobin gene is targeted in a human hematopoietic stem cell.

93 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human hemoglobin alpha 2 gene.

94 (previously presented). The method of claim 93, wherein said hemoglobin gene is targeted in a human hematopoietic stem cell.

95 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human MLH1 gene.

96 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human MSH2 gene.

97 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human MSH6 gene.

98 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human ApoE gene.

99 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human LDL receptor.

100 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human UGT1 gene.

101 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human APP gene.

102 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human PSEN1 gene.

103 (previously presented). The method of claim 70, wherein said targeted nucleic acid is the human PSEN2 gene.

104 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 1 - 160.

105 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 161 - 356.

106 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 357 - 500.

107 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 501 - 652.

108 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 653 - 1028.

109 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 1029 - 1128.

110 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 1129 - 1320.

111 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 1321 - 1432.

112 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 1433 - 1768.

113 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 4340, 1769 - 1799.

114 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 1800 - 2271.

115 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 2272 - 2775.

116 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 2776 - 2855.

117 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 2856 - 2979.

118 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 2980 - 3207.

119 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 3208 - 3343.

120 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 3344 - 3395.

121 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 3396 - 3471.

122 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 3472 - 3959.

123 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 3960 - 4035.

124 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 4036 - 4083.

125 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 4084 - 4319.

126 (previously presented). The method of claim 73, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 4320 - 4339.

127 (previously presented). The method of claim 73, wherein said oligonucleotide has sequence identical to any one of SEQ ID NOS: 1 - 4340.

128 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 1 - 160.

129 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 161 - 356.

130 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 357 - 500.

131 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 501 - 652.

132 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 653 - 1028.

133 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 1029 - 1128.

134 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 1129 - 1320.

135 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 1321 - 1432.

136 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 1433 - 1768.

137 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 1769 - 1799.

138 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 1800 - 2271.

139 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 2272 - 2775.

140 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 2776 - 2855.

141 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 2856 - 2979.

142 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 2980 - 3207.

143 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 3208 - 3343.

144 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 3344 - 3395.

145 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 3396 - 3471.

146 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 3472 - 3959.

147 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 3960 - 4035.

148 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 4036 - 4083.

149 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 4084 - 4319.

150 (previously presented). The method of claim 75, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 4320 - 4339.

151 (previously presented). The method of claim 75, wherein said oligonucleotide has sequence identical to any one of SEQ ID NOS: 1 - 4340.

152 (previously presented). The method of claim 78, wherein said oligonucleotide has at least three terminal phosphorothioate linkages.

153 (previously presented). The method of claim 152, wherein said targeted nucleic acid is the human ADA gene.

154 (previously presented). The method of claim 153, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 1 - 160.

155 (previously presented). The method of claim 152, wherein said targeted nucleic acid is the human beta globin gene.

156 (previously presented). The method of claim 155, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 357 - 500.

157 (previously presented). The method of claim 152, wherein said targeted nucleic acid is the human hemoglobin alpha 1 gene.

158 (previously presented). The method of claim 157, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 2776 - 2855.

159 (previously presented). The method of claim 152, wherein said targeted nucleic acid is the human hemoglobin alpha 2 gene.

160 (previously presented). The method of claim 159, wherein said oligonucleotide includes the sequence of any one of SEQ ID NOS: 2856 - 2979.

161 (currently amended). A method of targeted chromosomal sequence alteration of a chromosomal sequence present within a cell in vitro, the method comprising:

introducing a sequence-altering oligonucleotide into a cell in vitro,

wherein said sequence-altering oligonucleotide:

is a single-stranded nonhairpin oligonucleotide 17 - 121 nucleotides in length;

has an unmodified DNA domain of at least 8 contiguous deoxyribonucleotides;

is fully complementary in sequence to a first strand of the cell's chromosomal DNA at a chromosomal target sequence, except for one or two mismatches positioned (i) within said oligonucleotide's unmodified DNA domain and (ii) at least 8 nucleotides from said oligonucleotide's 5' and 3' termini; and

has chemical modifications consisting essentially of at least one terminal locked nucleic acid (LNA), or at least one terminal 2'-O-Me base analog, or at least three terminal phosphorothioate linkages, or combinations thereof, and

wherein said cell is not a human embryonic stem cell,

whereby said introduced oligonucleotide directs sequence alteration at said chromosomal target sequence by the cellular repair enzyme machinery.